anuric. A renal biopsy was performed after four days. It disclosed extracapillary glomerulonephritis, with crescents, which destroyed all glomeruli. Immunofluorescence showed, in addition to heavy fibrinogen fixation on crescents, linear IgG deposits on glomerular basement membrane. Four consecutive lupus erythematosus (LE) cell preparations were positive. Antinuclear antibodies were 1/2048. Anti-DNA antibodies were 102 U/ml by radioimmunologic detection. Antigen antibody complexes were detected by the labelled C1q technique. Anti-GBM antibodies were disclosed by radioimmunologic assay. They had a high affinity for GBM antigens. The evolution followed a rapidly fatal course, in spite of hemodialysis treatment, heparin, corticosteroid and cyclophosphamide therapy. No extrarenal signs or symptoms were noted. This case stresses the complexity of pathophysiologic mechanisms of human glomerulonephritis.

Experimental cystinuria-dibasic aminoaciduria: Implication for testing anticystinuric drugs. *J. Thomas, C. Charpentier, E. Thomas and A. Lemonnier. Unité 17 de l'INSERM (Pr. A. Monsaingeon), Hôpital Paul Brousse, Villejuif, Laboratoire Central de Biochimie (Pr. A. Lemonnier), Centre hospitalier de Bicêtre, Le Kremlin-Bicêtre.* Intraperitoneal injection, in the rat, of three dibasic amino acids—lysine, arginine or ornithine, 2,000 or 3,000 mg/kg of body wt—provoked a pathological elimination of cystine and of the three dibasic amino acids, moreover mixed disulfur of cysteine and homocysteine. This reproduced exactly the profile of human pathological cystinuria. This provoked cystinuria allows trial of anticystinuric drugs; D-penicillamine, α-mercaptopropionylglycine, sodium dithiosalicylate, well-known for their anticystinuric activity in man, were administered by i.p. injection, 150 mg/kg of body wt, 30 min before arginine injection (3,000 mg/kg of body wt): they considerably decreased cystine elimination. This method permitted us to find a similar action for the bis (hydroxy-2-ethylthio)-1-10 decane. Ingestion of that drug by cystinuric patients confirmed the results obtained in the rat.

Study of plasma renin activity, based on results obtained from 40 patients subjected to intermittent hemodialysis. *J. C. Valdenaire, C. Martineaux, N. de Talence and M. Kessler. Services de Néphrologie (Pr Cl. Huriet) et d'Exploratoins fonctionnelles rénales et métaboliques (Pr M. Boulange) du C.H.U. de Nancy, France.* This study is based on biological assays of plasma renin activity (PRA) in 40 cases of chronic renal failure treated by intermittent hemodialysis between 1972 and 1974. The authors have distinguished three clinical groups of patients: *I*) patients with normal blood pressure whose PRA was found to be normal, *II*) patients whose blood pressure was normalized by hemodialysis and whose PRA was found to be higher than in group I and *III*) patients with malignant arterial hypertension whose PRA was found to be significantly higher than in the other two groups ($P < 0.001$). The 40 subjects were also studied to determine the effect on PRA of one hemodialysis run: a statistically significant increase was observed in the case of patients in groups I and II. However, no variation was noticed in the case of patients in group III. In the case of 18 patients, repeated assays were carried out, but in two cases only was there evidence of an aggravation in the malignancy of the hypertension, with an increase in PRA, despite the use of intensive ultrafiltration. In 11 of the cases in group III, binephrectomy was undertaken with positive results in 8 cases.

Hemodynamics and water and sodium excretion in the blood-perfused isolated dog kidney: Effects of some prostaglandin-synthetase inhibitors. *J. L. Vanherweghem, J. Ducobu, A. D'Hollander and C. Toussaint. Laboratoire de Médecine Expérimentale, Université Libre de Bruxelles, Fondation Médicale Reine Elisabeth, Bruxelles, Belgium.* In the course of their perfusion with fresh heparinized blood, dog kidneys demonstrate progressive vasodilation (VD) with enhanced sodium (C_{Na}) and free water (C_{H_2O}) clearances. As these changes could be explained by the action of endogenous prostaglandins (PG), various PG-synthetase inhibitors were added to the 400 ml of blood perfusing one kidney, the contralateral organ serving as control, both kidneys being simultaneously perfused on two Nizet's pump-oxygenators. The PG-synthetase inhibitors tested were indomethacine (8 mg), naproxen (100 mg), lysine acetylsalicylate (LAS: 450 mg) and clopirac (100 mg). All compounds regularly inhibited VD, without affecting GFR. They also increased C_{Na} and decreased C_{H_2O}/V (an index of Na reabsorption in the ascending limb of Henle's loop) without affecting ($C_{Na} + C_{H_2O}$)/GFR (an index of the amount of filtered load of solutes which escaped proximal reabsorption). This latter ratio was, however, increased by larger LAS dosages (900 mg). Intrarenal circulation was analyzed by ^{141}Ce and ^{85}Sr microspheres in the course of the clopirac experiments. Blood flow in control kidneys steadily increased within outer (OC) as well as in inner cortex (IC), the intrarenal partition of both flows, initially favoring IC in comparison with kidneys *in situ* remaining unaffected in the course of perfusion (OC, 65%; IC, 35%). Clopirac reduced both OC and IC, the decrement being somewhat larger for IC (OC, 75%; IC, 25%). It is concluded that VD observed in the isolated kidney, which favors IC, is prevented by PG-synthetase inhibitors. Paradoxically, these drugs produce an important increase in Na excretion rate through inhibiting Na transport in Henle's loop and, at high dosages, in proximal tubule. This effect could be secondary to a direct tubular action, common to all four compounds, or would necessitate a revision of the role of PG on the tubular reabsorption of Na.

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Evidence for a viral etiology in endemic (Balkan) nephropathy. *K. Apostolov and P. Spasic, Hammersmith Hospital, London, England.* Renal biopsy specimens taken at operation from seven patients with clinically typical endemic (Balkan) nephropathy have been examined by thin sectioning and electron microscopy. The glomeruli showed mesangial changes, and the basement membrane was grossly thickened and convoluted. The renal tubules showed evidence of cell fusion and spongiform degeneration. Numerous cytoplasmic vesicles containing both free and apparently budding particles of size 80 to 200 nm were found. These particles bore the appearance of a coronavirus as seen by thin sectioning, and were similar in appearance to those seen in the kidneys of chickens infected with infectious bronchitis virus of fowls, which is also a coronavirus. It is suggested that the disease is, in fact, a slow virus infection of the kidney by a coronavirus, and data will be presented which suggest that the pig may be the primary source of infection.

Irreversible structural changes in intrarenal vessels associated with pregnancy: A clinical, histologic and angiographic study. *R. P. Burden, W. N. Boyd, K. Baker, M. O. Grant, T. H. Marshall and G. M. Aber. Department of Nephrology, North Staffordshire Royal Infirmary, Hartshill, Stoke-on-Trent, England.* The effect of certain complications of pregnancy (including preeclampsia and abruptio

placenta) on the histologic and angiographic appearances of the intrarenal vessels and on blood pressure and renal function have been studied in 20 patients in whom there was no evidence of preexisting hypertension or renal disease. Three months after the acute episode, all patients had angiographic abnormalities which included tortuosity, occlusions, irregularity of the lumen and stasis of contrast involving the interlobar and arcuate arteries. In the nephrogram there was evidence of peripheral ischemia, loss of the normal demarcation between cortex and medulla and cortical infarcts. Histologic abnormalities of the vessels were confined to thrombi in glomerular capillaries in two patients, and to reduplication of the internal elastic lamina in a third. At the time of the renal angiography and biopsy, 33% of patients had impairment of creatinine clearance and 25% were hypertensive (diastolic blood pressure, 90 mm Hg or more). Patients were followed for periods of up to five years (mean, three years) and during this time there was no further deterioration in renal function although 50% of the total had become hypertensive. Although the severity of the abnormalities of the intrarenal circulation bore a close relationship to the degree of microangiopathy which occurred during the acute obstetric complication, i.e., being more severe in patients with abruptio placenta, established hypertension was less common in this group.

Prognosis, disease activity and immunologic tests in lupus nephritis. *J. S. Cameron, N. G. P. Slater, D. R. Turner, B. D. Williams C. S. Ogg, D. G. Williams and M. H. Lessof. Departments of Medicine and Pathology, Guy's Hospital, London, England.* A number of tests have been suggested to be useful predictors of outcome in lupus nephritis. These include the appearance of renal biopsy specimens, serum complement concentrations and a variety of tests based upon the presence, quantity or quality of circulating antibody against native double-stranded DNA. We have studied sera from 99 patients with clinical evidence of lupus nephritis, of whom 65 had a renal biopsy. Data from 51 biopsied patients with at least one year's follow-up have been analyzed in detail. Serial complement (C3 and C4) concentrations have been accumulated and DS-DNA binding has been measured by the Farr method. Both the counter-immunoelectrophoresis test for precipitating DNA antibody and the recently described *Crithidia luciliae* kinetoplast assay have also been examined retrospectively. The clinical activity at each attendance or admission was evaluated serially at nearly 300 points in 32 of the biopsied patients with two years' follow-up using a seven-point scale. At onset, the best predictor of outcome is the appearance of the renal biopsy specimen; although evolution from mild appearances to severe nephritis has been observed in five individuals, and some patients with severe histologic appearances have done well. Although the DNA binding and kinetoplast assays had high *diagnostic* precision, neither the degree of DS-DNA binding nor the kinetoplast titer correlated well with *clinical activity* (of renal disease) in the majority of patients. Correlation between C4 concentrations and activity was better. Correlation between C3 and C4 and DNA binding or kinetoplast titers were also poor. Suppression of immunologic activity, as judged by these tests, may be both unnecessary and dangerous in some patients; clinical and histologic criteria still remain the best guide for treatment.

Silicon and the kidney. *J. W. Dobbie, M. J. B. Gray and A. C. Kennedy. Tenovus Kidney Diseases Research Unit, and the University Department of Medicine, Royal Infirmary, Glasgow, Scotland.* Suspicion of silicon as a potential nephrotoxic agent in man comes from its possible role as an etiologic factor in endemic nephropathy (Marcovic BL, Arambasic MD: *J Pathol* 103:35, 1971) and from earlier work on the incidence of renal lesions in silicosis (Saita G, Zavaglia O: *Med Lav* 42:41, 1951; Kolev K, Doitschinov D, Todorov D: *Med Lav* 61:205, 1970). However, the lack of a simple, reliable method of measuring silicon in biological fluids has so far hindered any comprehensive study of silicon metabolism in man. This paper describes *a*) the successful application of atomic absorption spectroscopy to the measurement of urinary silicon; *b*) the determination of mean daily excretion of silicon in 45 healthy young adults (mean, 7.44 mg of Si/24 hr; SD, 3.54); *c*) a significant rise in urinary excretion of silicon (3- to 38-fold increase) in a group of 14 young adults following ingestion of 5 g of magnesium trisilicate B.P.; *d*) A separate series of investigations in which the nephrotoxicity of silicon was investigated in the experimental animal. Three silicon-containing compounds (magnesium trisilicate B.P., crushed quartz and crushed Arran granite) were added to the drinking water (250 mg/liter) of three groups of male guinea pigs for four months. At autopsy, all animals receiving magnesium trisilicate and two animals receiving crushed quartz showed focal interstitial nephritis. In view of the increasing exposure of Western man to silicate food additives, the present findings suggest that the potential nephrotoxicity of silicon merits further study.

The treatment of the refractory anemia of nephrectomized hemodialysis patients with cobalt chloride. *J. M. Duckham and H. A. Lee. Wessex Renal Unit, St. Mary's General Hospital, Portsmouth, England.* Anephric patients on routine maintenance hemodialysis have received therapeutic trials with small doses of enteric coated cobalt chloride. Six of eight patients who completed the first trial with enteric coated cobalt chloride, 50 mg daily for 12 weeks, showed a significant rise in hemoglobin concentration of over 25% during therapy and a fall to near pretherapeutic levels when cobalt was withdrawn. The improvement in hemoglobin concentration was reproducible and could be maintained with doses of 25 mg of cobalt chloride daily. With longer periods of treatment, the hemoglobin concentration could be improved by up to 70%. Four of the patients showed a definite diminution in their blood transfusion requirements and three experienced a definite sense of increased well-being during treatment. Only one patient was unable to complete a trial of therapy due to gastrointestinal side effects and it is possible that one patient developed reversible high tone hearing loss due to the toxic effects of cobalt after 56 weeks of treatment. Serum cobalt levels tended to stabilize after two months' continuous treatment in the therapeutic range of 40 to 100 μg/100 ml. A rapid fall in serum cobalt was seen on cessation of treatment. Having gained a good response with cobalt chloride, 50 mg daily for 12 weeks, it is suggested that an intermittent course of cobalt can be given or the dose can be reduced to a maintenance dose of 25 mg daily. Using these dose regimes we do not anticipate unwanted side effects of therapy, particularly as cobalt is dialyzable.

Avascular necrosis of bone following renal transplantation. *K. M. Hawking, B. F. van den Bosch and J. M. Wilmink. University Hospital Dijkzigt, Department of Internal Medicine I and Department for Orthopaedic Surgery, Erasmus University (EU), Rotterdam; and Department of Medicine, Wilhelmina Gasthuis, Amsterdam, The Netherlands.* Avascular necrosis of bone (AVN) is a common complication of otherwise successful renal transplantation, occurring in 5 to 37% of recipients in most reported series. Fifty-five patients received cadaver renal allografts at EU between May, 1971 and January, 1975. Forty-four of these had functioning grafts for nine months and longer, 18 of these (41%) developed AVN between 130 and 700 days after transplantation. Seven patients have needed orthopedic surgery (ten hip replacements, one Marmar knee prothesis and one knee exploration) for severe pain or disability. At the Renal Transplantation Unit, Wilhelmina Gasthuis, Amsterdam, the incidence of AVN is lower, and the disease less severe. Between 1968 and January, 1975 58 patients received 61 transplants. Forty-one (71%) of these had renal function for more than nine months, and only six of these (15%) developed AVN. One patient had severe pain and needed orthopedic surgery. Patients, kidneys and doses of prednisone received were similar at the two centers. Among the recipients at EU, no differences were found between patients with subsequent AVN and those without with respect to age or sex of recipient or donor,

duration of dialysis before or after transplantation, method or duration of preservation of the donor kidney or amount of prednisone received. Twelve of the 16 patients (75%) living in the immediate vicinity of Rotterdam developed AVN as compared to six of 28 (21%) living elsewhere. This suggests than an environmental factor, such as water supply, may be contributing to the high incidence of AVN at EU.

Plasma-exchange and immunosuppression in the treatment of Goodpasture's syndrome. *C. M. Lockwood, A. J. Rees, Pamela Ewan, D. K. Peters and C. B. Wilson. Department of Medicine, Royal Postgraduate Medical School, London, England; and Department of Experimental Pathology, Scripps Clinic and Research Foundation, La Jolla, California.* Eight patients with Goodpasture's syndrome, all of whom had demonstrable circulating antibody to glomerular basement membrane (GBM) as detected by radioimmunoassay, were treated by a regime of intensive plasma-exchange, cytotoxic drugs and steroids. Four patients had some renal function at presentation and in three of these there was improvement in renal function and termination of anti-GBM antibody synthesis following this therapeutic regime. The fourth patient, at present in the second week of treatment, is showing improvement in renal function and fall in anti-GBM antibody titer. The other four patients were anuric at presentation and all had extensive changes on renal biopsy. No return of renal function occurred in this group and anti-GBM antibody levels, although reduced by the combination of plasma-exchange, cytotoxic drugs and steroids, remained elevated. Pulmonary hemorrhage was a feature at presentation in six patients and in one was severe and life-threatening. In this patient and four others, lung bleeding was arrested soon after the start of therapy. In a further patient, currently undergoing therapy, hemoptysis has stopped after one week's treatment. The "deglobulinating" effect of plasma-exchange using purified protein fraction, leading to depletion of fibrinogen, complement and immunoglobulins will be discussed.

Clofibrate-induced muscle damage in patients with chronic renal failure. *A. M. Pierides, F. Alvarez-Ude and D. N. S. Kerr. Department of Medicine, University of Newcastle upon Tyne, England.* Four patients in chronic renal failure who were given 1 to 2 g of clofibrate daily developed a hypercatabolic state and a clinical syndrome characterized by widespread muscle weakness and tenderness, particularly affecting proximal muscles. Muscle enzymes such as creatinine kinase rose significantly to up to 8,000 U/liter. Two patients with advanced but static renal failure (serum creatinine, 9 to 12 mg/100 ml) deteriorated rapidly with a rise in serum urea and creatinine and required early dialysis. Renal function did not recover in these two patients when clofibrate was withdrawn and at present one of the patients continues on regular hemodialysis while the other patient, who was a poor regular hemodialysis patient, died a few weeks later. One patient with mild renal failure (serum creatinine, 3.5 mg/100 ml) recovered fully when clofibrate was withdrawn. One anephric patient already on regular hemodialysis developed the clinical syndrome and also a marked paradoxical rise in cholesterol and fasting triglycerides up to 3.5 g/100 ml. Serum chlorophenoxyisobutyric acid (CPIB), the circulating active metabolite of clofibrate, was estimated serially in two of the patients and was found to be markedly elevated, outside the therapeutic range. It is thought that high serum levels of this compound are responsible for the observed side effects. It is suggested that uremia leads to accumulation of CPIB with a rise in the free circulating fraction. Under these circumstances, clofibrate should be used very cautiously indeed, ensuring an appropriate reduction in dosage according to residual renal function. Regular monitoring with serum muscle enzymes and CPIB are advisable.

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Efficacy of petroleum charcoal hemoperfusion and acetate-free dialysate in eight patients with hepatic coma. *I. Amano, H. Kano, S. Iwatsuki, H. Takahira, K. Ohta and K. Maeda. Chukyo Hospital and The Biodynamics Research Institute, Nagoya, Japan.* Although the pathogenesis of hepatic coma is complicated, we have tried to save patients by eliminating encephalogenic substances and correcting electrolytes and pH. Our artificial liver assist is a combination of petroleum charcoal hemoperfusion and hemoperfusion using acetate-free dialysate. The feature of petroleum pitch charcoal is that it releases small amounts of 1.2 to 5.0 μ pulverized carbon. It shows excellent adsorption *in vitro* for methionine of amino acids, short chain fatty acid and some annuli amins. Two cases of eight patients were advanced posthepatic cirrhosis and one of them had a porta caval shunt. The remaining six cases were fulminant viral hepatitis. Seven of the eight patients with grade 3 to 4 coma recovered consciousness and three of them survived. Dialysate was free of acetate which was affected more by charcoal adsorption than bicarbonate. Bicarbonate contained in dialysate could correct pH stabler than acetate. Our experience shows that independently the charcoal hemoperfusion and the body fluid correction device cannot be effectively used. Reproduction of liver tissues, in histological study, was observed in spite of considerable hemoperfusion as many as ten times. No emboli of pulverized carbon were seen in the lungs, liver, spleen or kidneys.

A full account of the meeting will appear in the Proceedings of the EDTA by January 1976. AB Gambro (Sweden) has kindly assisted with the publication of the abstracts. Only those abstracts that have been selected for presentation are included.

Accumulation and excretion of middle molecules. *H. Asaba, J. Bergström, P. Fürst and L. Zimmerman. Department of Nephrology, S:t Eriks sjukhus, Stockholm, Sweden.* There is evidence that potentially toxic middle molecules (MM) accumulate in uremia, but little is known about their rate of generation and excretion. By using gel filtration combined with gradient elution chromatography, we evaluated quantitatively the concentration of MM fractions (7a, b, c) from the integrated peak areas of the chromatograms. Plasma and urine from patients with varying degrees of renal failures were analyzed. Among 85 patients studied, measurable plasma peaks were only found when serum creatinine was above 6 mg/100 ml or creatinine clearance (K_{cr}) below 10 ml/min. No correlation was found between serum urea and serum creatinine and the accumulation of fraction 7a, b or c. There was a linear correlation between K_{cr} and the renal clearance of 7a, b and c (K_{7a}, K_{7b}, K_{7c}). K_{7b} and K_{7c} were on average equal to K_{cr}; K_{7a} was higher indicating either some tubular excretion or production by the kidney. The rates of excretion of individual MM in the urine varied considerably among different patients; peaks found high in plasma were also found high in the urine. Taking excretion rate to be equal to generation rate, the results indicate that great differences in production (by a factor of 5 or more) are more important for the accumulation of MM than passive retention. This also explains the lack of correlation with serum urea and serum creatinine. In consequence, mathematical models for calculating the level of MM based on the assumption of a constant production rate will give erroneous results.

Wrist watch-size single-needle clamping device. *R. A. Baillod, C. M. Roberts, J. F. Moorhead, Z. Varghese and A. Peacock. Renal Unit, Royal Free Hospital, London, England.* Recent technical ad-